AdAlta
next generation protein therapeutics

Next generation protein and cell therapies: solutions to debilitating diseases

Tim Oldham PhD, CEO and Managing Director, AdAlta (ASX:1AD)

Overview for investors, 13 July 2023

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AdAlta business and focus

Purpose: going where antibodies cannot to address debilitating diseases

Producing a high-value, next generation protein and cell therapy product pipeline for diseases where traditional antibodies are ineffective

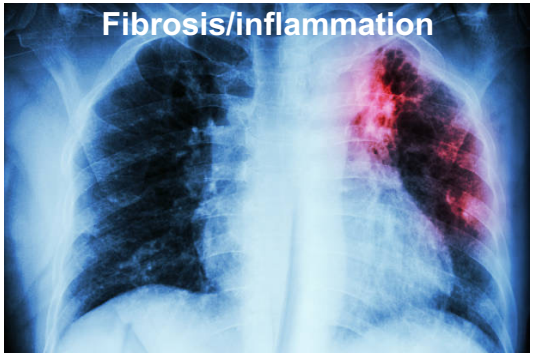
Discovery business

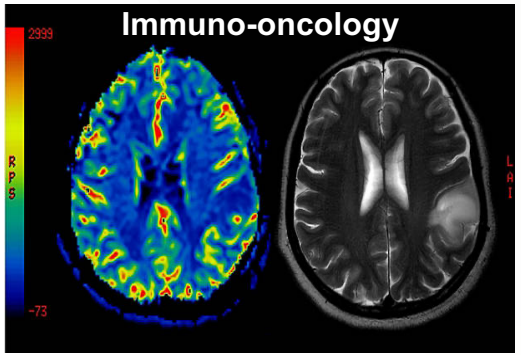
Multiple high value product candidates for development or licensing

i-body® platform
+
In-house discovery team

Product development business

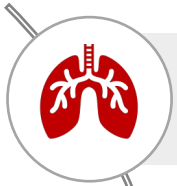
Candidates progressed through value-adding development milestones for out-licensing or co-development





Experienced leaders, in-house protein engineering
+
Cost effective Australian location

AdAlta's portfolio: high value therapeutics and a platform to help other companies address challenging diseases in fibrosis and immuno-oncology



Fibrosis: degenerative, progressive, fatal

AdAlta's AD-214 could meet a desperate need for new approaches for debilitating diseases of the lung (US$4.3b), kidney (US$10b) and eye (US$15b)

Comparator licensing transactions: >$45m up front; >$320m milestones

CAR-T cell therapy providing new hope… for blood cancer patients so far

AdAlta and Carina's i-CAR-T cells could offer same hope for patients with solid tumours (US$20b by end of decade)

Comparator licensing transactions: >$10m up front; >$300m milestones

Immuno-oncology drugs revolutionising cancer treatment… for some

AdAlta and GE Healthcare's GZMB i-PET imaging agent could identify responders early (US$6b)

Comparator product revenue potential: ~$400m pa

Antibodies cannot do everything!

AdAlta's i-bodies® are a differentiated drug discovery platform for difficult diseases that partners can leverage

AD-214 program

The need: Idiopathic Pulmonary Fibrosis (IPF)

Scarring of the lungs reduces lung function:
irreversible, unpredictable, incurable

>490,000 people living with IPF[2]

>**40,000** people die every year

3.8 years median survival

88% aged 55 or older

Two current therapies had **US$4.3b sales** in 2022[2] …

… despite limited effectiveness, serious side effects

Many other fibrosis market opportunities
- Almost every organ: eye (**US$15b**), kidney (**US$10b**), cancer (**US$1b** per indication)[3]
- "Long COVID" is a developing issue – further increasing the need for better anti-fibrotic drugs[1]
- Re-emergence of silicosis

[1] PM George, et al, "Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy", Lancet published online May 15, 2020.
[2] GlobalData, Idiopathic Pulmonary Fibrosis: Competitive Landscape, April 2023
[3] GlobaData, disease analysis reports

AdAlta's solution: AD-214 is being readied for Phase II clinical studies and partnering

AD-214: strong value proposition built so far

First in class molecule targeting validated mode of action
- ✓ Competitively positioned

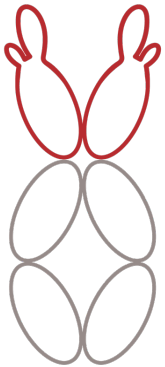
Pre-clinical efficacy in multiple animal models of fibrotic disease
- ✓ Multiple indication potential

Manufacturing process established
- ✓ Major investment done

Phase I successfully completed
- ✓ Well tolerated, evidence of target binding

Clinically viable dosing regimen
- ✓ Bridge between pre-clinical efficacy and Phase I results

Strong intellectual property, regulatory position
- ✓ Patents protecting asset to 2036
- ✓ US FDA Orphan Drug Designation for IPF



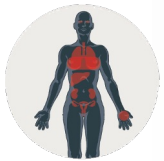
Next steps to advance to Phase II

Phase I extension study H2 2023
- Extend safety to higher, target doses for Phase II
- Add data to inform partnering

Partnering discussions accelerating
- Potential for substantial return on investment
- Non-dilutive funding to advance to Phase II
- Preclinical investments to support diligence

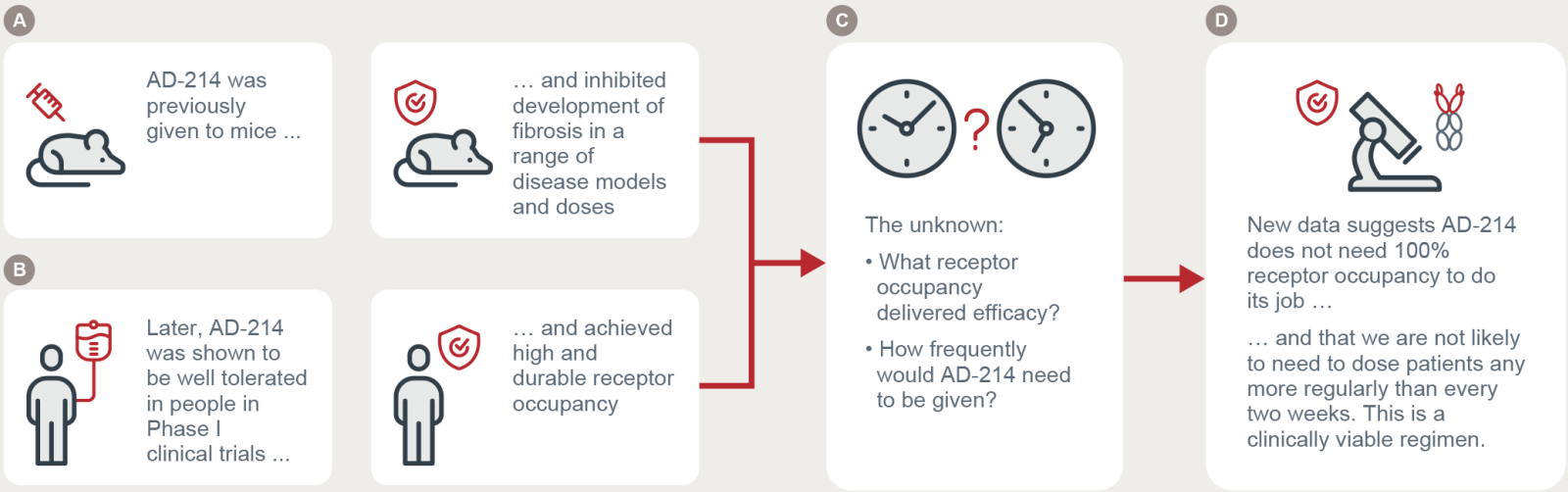
Planning and preparing for Phase II IV clinical trials (lung or kidney fibrosis)
- Phase II manufacturing, toxicology study slots booked
- Working well with vendors to maintain speed AND flexibility



Sources: GlobalData; www.clinicaltrials.gov (accessed 7 and 17 October 2022)

Potential for efficacy at clinically viable dosing regimen demonstrated



A. AD-214 has demonstrated efficacy in multiple animal models of fibrotic disease
B. In humans, AD-214 was able to maintain more than 60% receptor occupancy (blocking) for up to three weeks after IV infusion, depending on dose

C. Is this sufficient to achieve efficacy, given at least two weeks between IV doses is required for clinical viability?

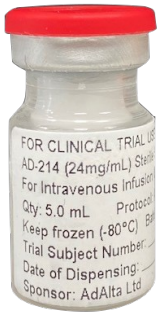
D. YES – new data shows that AD-214 does not require 100% receptor occupancy to meaningfully inhibit a model fibrotic process: efficacy of two weekly or longer dosing regimens is plausible

Source: ASX release 7 July 2023

Phase I extension study delivers new data in 2023 to support partnering and Phase II

AD-214 multidose Phase I extension clinical study

- Evaluating safety, PK and PD of multiple 10 mg/kg doses
- Similar design to prior Phase I study
- Utilises existing AD-214 inventory
- Top line data end-2023



Establishes safety of AD-214 at likely maximum dose to be used in Phase II studies

✓ *Shorter dose escalation stage, reduced cost in Phase II study*

Further explores PK, PD and safety trends observed in Phase I

✓ *Strengthens safety profile*

✓ *Better informs dosing levels and schedule for Phase II*

Enhances partnering process

✓ *Additional data to address known and potential questions*

✓ *Maintains product development momentum*

The value: pharma companies license fibrosis assets for significant prices: IPF examples

Date	Licensor/target	Licensee/acquirer	Transaction	Upfront payment to licensor	Contingent milestones	Clinical Phase at transaction
Aug-22	KINIKSA	Genentech, A Member of the Roche Group	License	**US$80m**	US$620m	2
Nov-19	Promedior	Roche	License	**US$390m**	US$1,000m	2
Nov-21	BLADE THERAPEUTICS	BIOTECH ACQUISITION COMPANY	Acquisition	**US$254m**	N/A	2 (Ready)
Nov-21	OncoArendi Therapeutics	Galápagos	License	**Not disclosed**	€320m	2 (Ready)
Sep-21	Syndax	Incyte	License	**US$152m**	US$602m	2 (Ready)
Feb-21	泰德制药 TIDE PHARMACEUTICAL	GRAVITON BIOSCIENCE CORPORATION	License	**Not disclosed**	US$517.5m	1
Jul-19	bridgebio	Boehringer Ingelheim	License	**€45m**	€1,100m	1
Oct-22	DJS antibodies	abbvie	Acquisition	**US$255m**	Not disclosed	Pre-clinical (+ platform)

AD-214 almost Phase II ready

Source: Company press releases

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Co-developed immuno-oncology programs: i-CAR-cell therapies

The need: multifunctional CAR-cell therapies

Therapy involves re-engineering patient's own immune cells so they "see" cancer as a pathogen – **living drug, single dose, potentially curative**

>US$2.6 billion earned in 2022[3]

US$20.3 billion CAR-T market forecast for 2028[1]

6 FDA-approved CAR-T therapies since 2017 … but so far only for blood cancers

90% of cancers are solid tumours: harder to target, harder to access, immune suppressive … needs new multifunctional CAR cell therapies

>50% of CAR-T revenues from solid tumours by 2030[2]

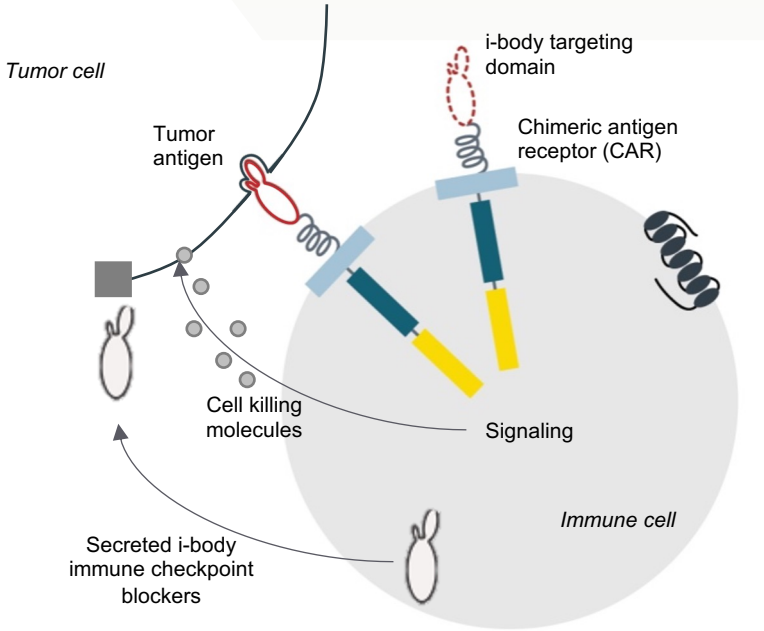
1. Grandview Research, "T-cell Therapy Market Size, Share & Trends Analysis" Feb 2021
2. Polaris Market Research, "CAR-T Cell Therapy Market Share, Size Trends, Industry Analysis Report", June 2021
3. Company websites and financial filings

AdAlta's solution: i-bodies enable superior CAR constructs (i-CARs) when combined with partner platforms

Tiny i-bodies take up LESS room in inserted gene, enabling TWICE the engineered functionality

Results in superior, multifunctional i-CAR products

- **Targeting**: novel tumor antigens
- **Targeting**: Dual and bi-specific CARs for enhanced specificity, reduced tumor escape
- **Persistence**: overcome immune suppression "checkpoints"
- **Performance**: stimulate immune cells, enhance trafficking and overcome "exhaustion"



First partnership established with Carina Biotech – up to 5 targets

Significant industry interest (from potential additional partners) in using i-bodies for targeting CAR cells

i-CAR-T assets: Carina co-development collaboration status

AdAlta and Carina are combining i-bodies and a world class CAR-T platform to create i-CAR-Ts that could offer improved precision, performance and persistence

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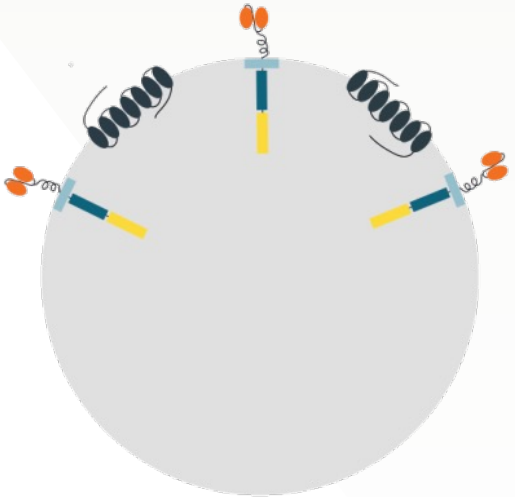
carina biotech

- ✓ i-body enabled CAR-T (i-CAR-T) cells have successfully demonstrated *in vitro* cancer cell line killing (lysis)[1]
- ✓ Target A: 9 A-i-CAR-T cells screened *in vitro* against cancer cell lines, 3 to progress to more extensive *in vitro* screens and *in vivo* proof of concept H1 2023
- ✓ Next two targets (targets B and C) to commence i-body discovery in Q2 2023



1. ASX release 29 November 2021

i-CAR-T: Valuable cell therapy partnering potential at pre-clinical proof of concept

AdAlta i-bodies + Carina cell therapy platform = i-CAR-Ts for solid tumor patients

3 of 5 programs underway; 1 entering proof of concept

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Significant industry interest from potential additional partners; value could be realized at preclinical PoC

Date	Licensee	Licensor	No. of assets	Upfront/target (US$m)	Deal value/target (US$m)
Jun-22	Bristol Myers Squibb	immatics	2	30	730
Jul-20	SANOFI	Kiadis pharma	1	20	988
Feb-20	GSK	immatics	2	25	300
Nov-19	Allogene	Notch THERAPEUTICS	1	10	304
Oct-18	Roche	sozBIOTECH	1	45	1702
Median value				**25**	**730**

Source: GlobalData, company press releases, AdAlta analysis

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Co-developed immuno-oncology programs: i-PET imaging

The need: Immuno-oncology (I/O) imaging

Immuno-oncology (I/O) drug market is worth **US$95 billion**[1] …

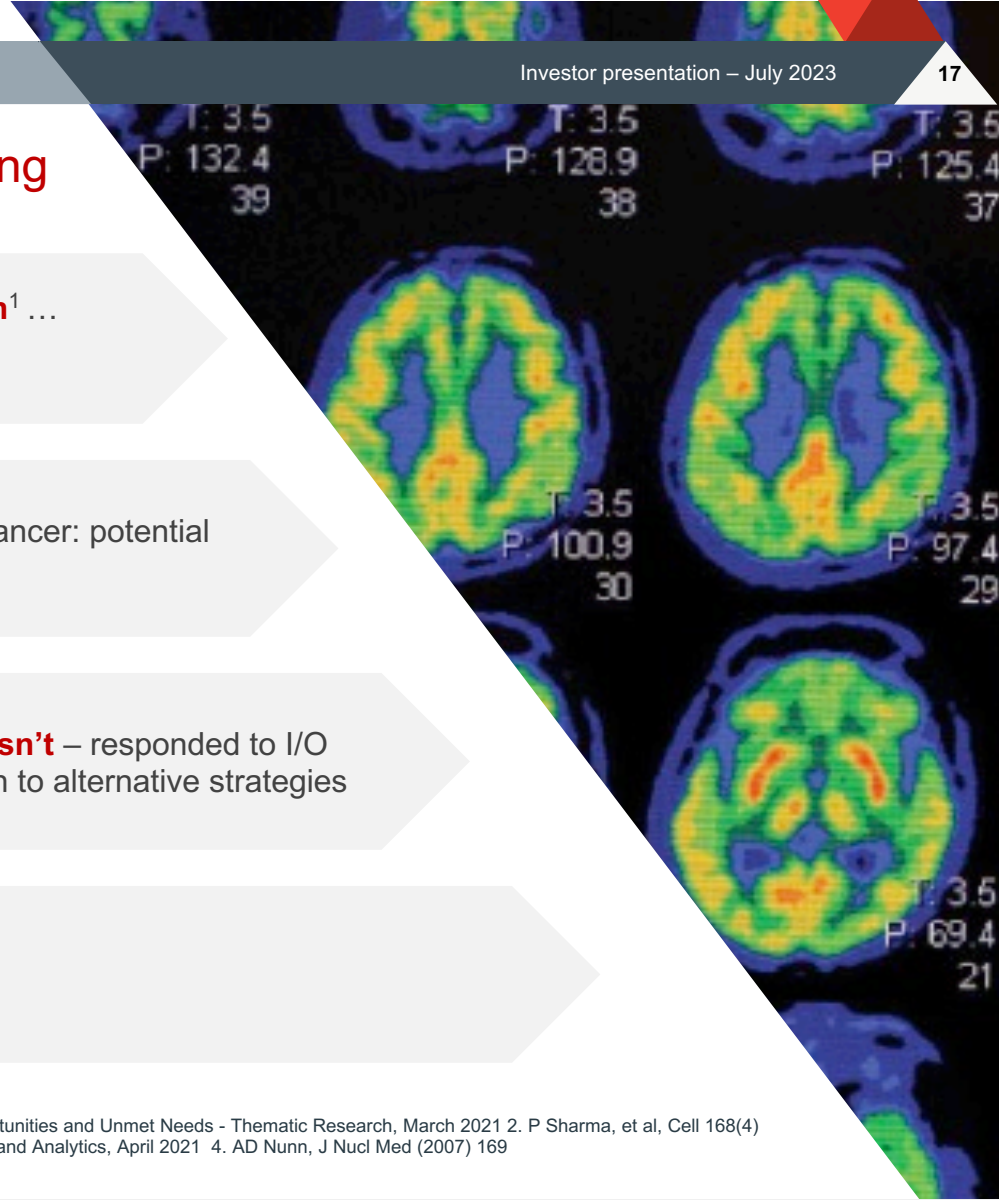
… but only **20-40%** of patients respond[2] to therapy

Granzyme B (GZMB) is produced by immune cells to kill cancer: potential biomarker of I/O drug activation of the immune system

PET imaging GZMB could help identify **who has – and hasn't** – responded to I/O drugs before their tumor progresses: enabling timely switch to alternative strategies

US$6.4billion[3] PET imaging agent market

>US$400m[4] annual sales for largest products



1. 2026 forecast by ResearchandMarkets.com, Immuno-Oncology - Market Analysis, Trends, Opportunities and Unmet Needs - Thematic Research, March 2021 2. P Sharma, et al, Cell 168(4) 707 (2017) 3. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021 4. AD Nunn, J Nucl Med (2007) 169

AdAlta's solution: funded discovery, shorter timeline to royalties for GZMB i-PET imaging asset

AdAlta i-bodies + GE PET technology = GZMB i-PET asset to evaluate the effectiveness of immuno-oncology drugs

AdAlta next generation protein therapeutics | GE Healthcare

- ✓ Fully funded discovery program plus downstream milestones, royalties
- ✓ i-body optimization, manufacturing development, pre-clinical proof of concept studies continuing
- ✓ Shorter time to royalty revenue than therapeutic product development
- \- Further updates as commercially relevant milestones are achieved

Market feedback confirms value and importance of this target

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The investment opportunity

i-bodies are a powerful drug discovery tool to engage targets that are intractable for traditional antibodies

Small Molecules

Avoid off-target issues of small molecules

Antibodies

~10% the size of human antibodies

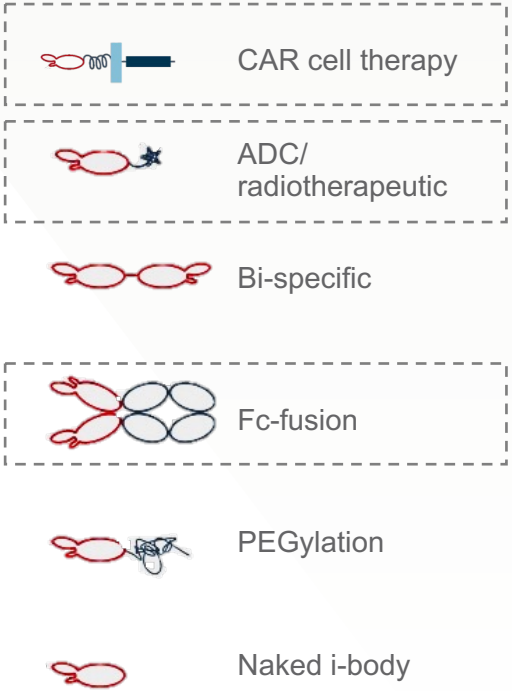
Enables access to novel targets and efficient payload delivery

i-bodies™

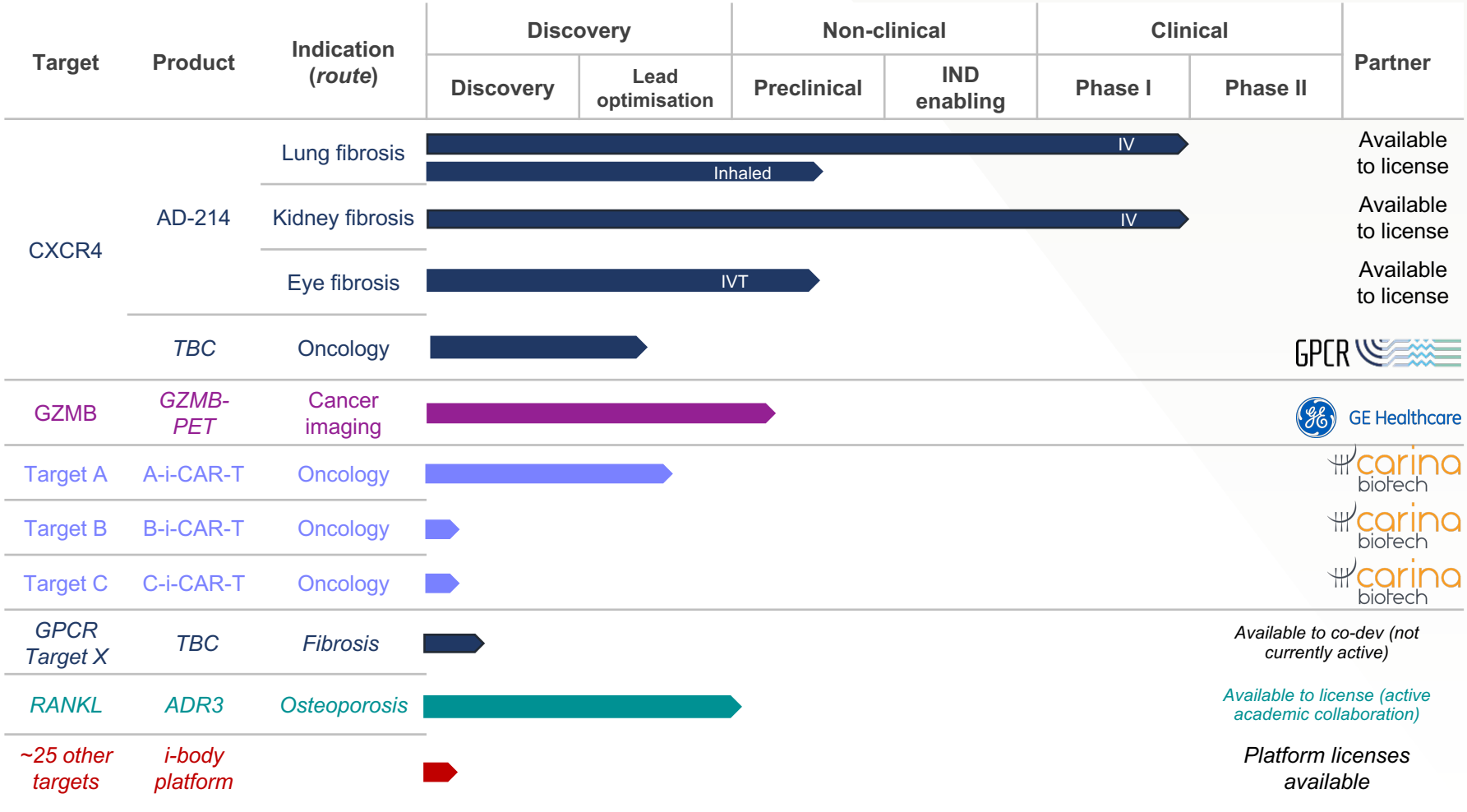
Unique binding capabilities drive unique pharmacology

Flexible, modular formats

Current pipeline focus



AdAlta's pipeline so far: five active assets plus additional partnering opportunities



Three partnering initiatives to generate return on investment

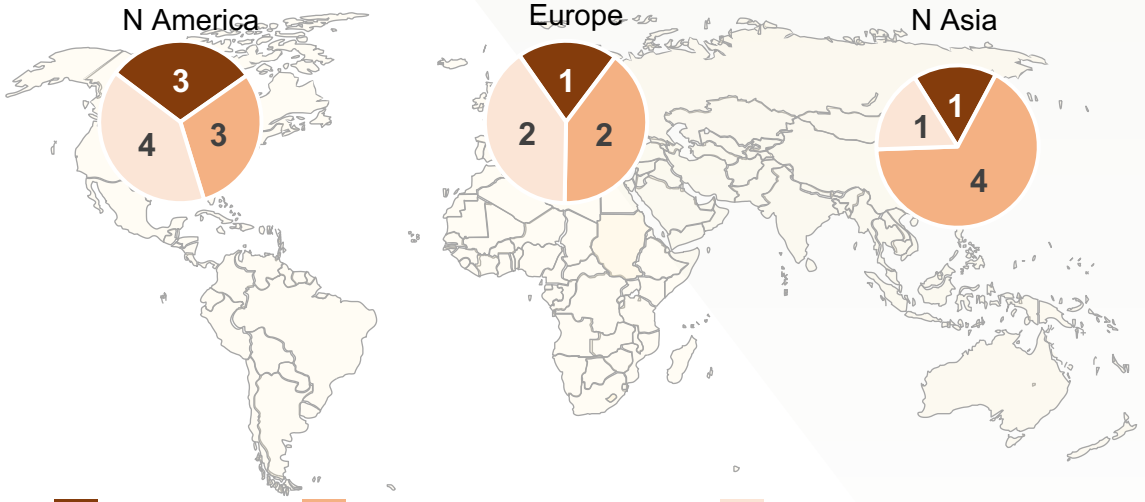
Slate of partnering initiatives

1. Out-licence AD-214
2. Out-license i-body discovery platform
3. Access complementary, near to clinic assets

Advisors

Grannus Securities
TUNGSTEN
lingmed 灵麦医药
MOTIONHALL

AD-214 partnering prospects by stage[1]



Under CDA:	Initial commercial and technical evaluation complete, detailed technical evaluation under confidentiality agreement in progress
Active technical evaluation:	R&D team have evaluated non-confidential data package and begun technical diligence calls with AdAlta
Commercial evaluation:	Business development team has confirmed strategic alignment and with search and evaluation team are evaluating detailed non-confidential data package

Excludes prospects that have communicated “pass” or “will wait until Phase II data is available”

[1] Source: June 2023 internal board report post BIO23; location based on company HQ

Upcoming CY2023 milestones: AD-214 and i-CAR-T data + multiple transaction upside potential

Strategy	Milestone	Impact
Realise value of AD-214	• HREC approval, 1st participant Phase I extension (Q3 23) • Headline results Phase I extension (Q4 23) • Progress existing partnering discussions (through 2023)	*Generates new data for partnering, shortens Phase II study* *Potential first major ROI (return on investment)*
Extend i-CAR programs	• A-i-CAR-T *in vivo* efficacy studies (H2 23) • Commence discovery on Carina A, B targets (Q2 23) • Progress co-development discussions (through 2023)	*Preclinical PoC; opportunity for early ROI* *Carina pipeline expansion – future value* *Potential non-dilutive financing for future programs*
i-PET progress	• Lead candidate preclinical efficacy (timing not forecast)	*Visibility to product potential, time to royalties*
Invest in i-body™ platform	• i-body2.0 and research excellence program • Evaluate synergistic technology, product transactions	*Maintain competitive advantage* *Expand clinical stage pipeline, accelerate growth, leverage costs and capabilities*

Corporate snapshot

Key financial details (12 July 2023)

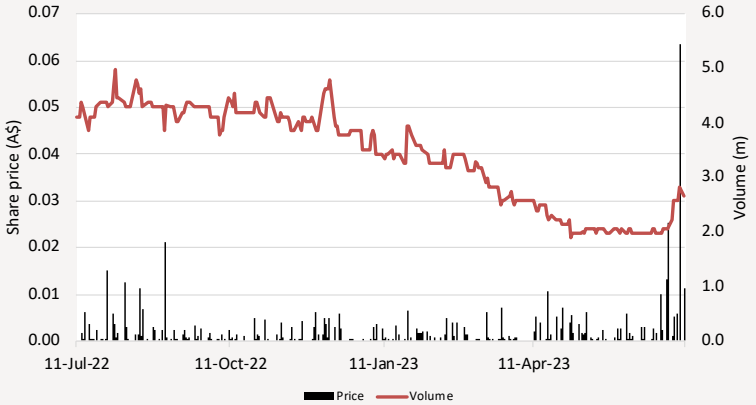
HQ and operations	Melbourne, Australia
Market capitalisation	**A$13.2m**
Share price (12 month closing range)	A$0.03 ($0.022 - 0.058)
12 month return	(35)%
Ordinary Shares (daily volume)	441,526,298 (170,651)
Listed Options	78,075,186
Unlisted Options	14,184,060
Cash (30 June 2023)*	**A$5.57m**

Largest shareholders (12 July 2023)** %

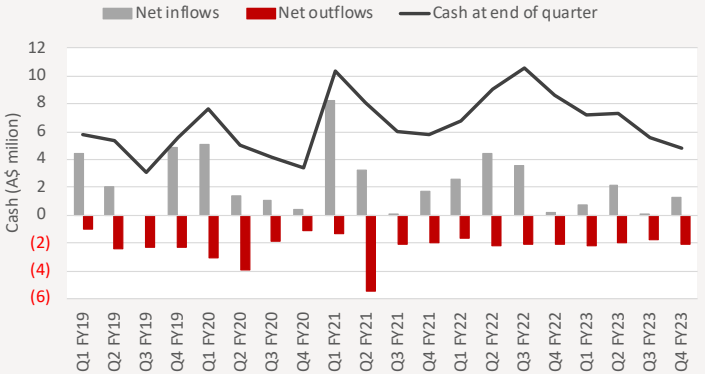
Platinum International Healthcare Fund	18.7
Meurs Group	14.6
FMI Pty Ltd atf Commonwealth of Australia	7.4
Sacavic Pty Ltd	5.9
Radiata Super Pty Ltd	4.3
HB Biotechnology Ltd	1.8
Other (1,358 total holders)	*47.3*
Total	**100%**

* Excludes additional A$1.82m raised received in July from oversubscribed rights offer announced 28 April 2023; a $4m loan facility with Victorian Government is secured by, and payable on receipt of, FY23 R&D Tax Incentive rebate, anticipated Q4 2023
** Non-diluted and excluding impact of 74.8m shortfall shares issued on 12 July 2023

Share price performance (ASX:1AD) (last 12 months)



Quarterly cash flows (A$ million)



Experienced, in-house team to execute from discovery through product development

BOARD

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PULMONARY DRUG DISCOVERY & DEVELOPMENT

IN-HOUSE DISCOVERY & DEVELOPMENT TEAM

8 PhD Staff + La Trobe Uni location
Skills in protein chemistry, i-body discovery, product development, pre-clinical development

Investment proposition

i-body platform to create value

Strategy: invest to maintain competitive advantage

Fibrosis/inflammation
AD-214: Phase II and partnering in $4.3b market[1]

Strategy: realise return on investment

Immuno-oncology
2 co-development collaborations (4 programs) in $20b[2] and $6b[3] markets

Strategy: progress and extend collaborations

Demonstrated product development and partnering expertise

"Blue sky" inorganic growth opportunities

AD-214 outlicensing
Additional platform transactions
Synergistic technology, product transactions

Steady news flow

Attractive current valuation with upside

1. GlobalData, Idiopathic Pulmonary Fibrosis Competitive Landscape, April 2023; kidney and eye fibrosis markets are larger 2. 2028 forecast by Grandview Research, "T-cell Therapy Market Size, Share & Trends Analysis" Feb 2021 3. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021

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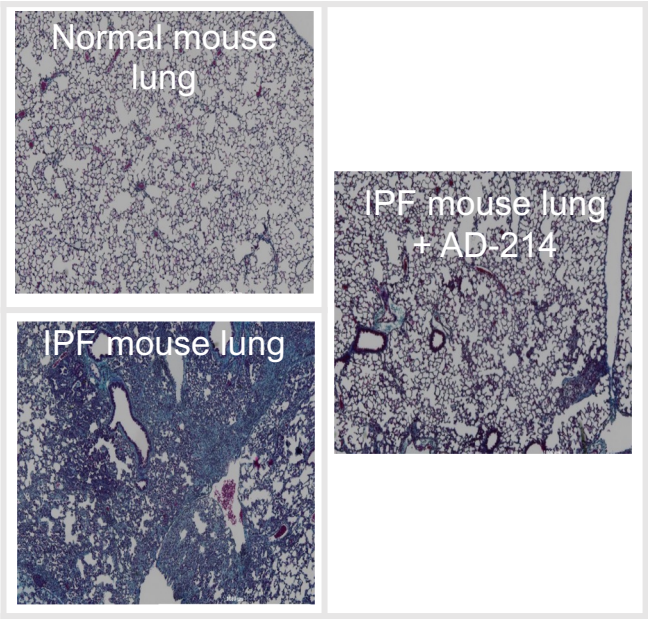
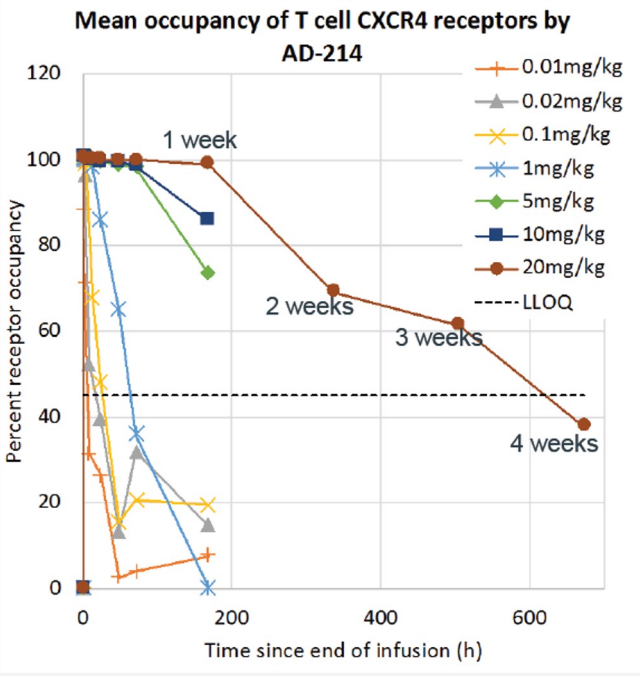
AD-214: efficacy validated in IPF mouse model; safety and target engagement in Phase I

AD-214 inhibited development of lung fibrosis in a mouse model at a wide range of doses and dose intervals[1]



AD-214 was well tolerated in Phase I clinical trials and demonstrated high and durable receptor occupancy[2]



[1] Murigenics_20210208. (Fibrosis induced by bleomycin at day 0; treatment commenced day 8; images from 10 mg/kg AD-214 every 4 days; statistical significance assessed using ANOVA and post-hoc Dunnett's test; ns (not significant) = p >0.05, * = p<0.05, ** = p < 0.01 relative to 21-day bleomycin vehicle; negative control is an i-body that does not bind specifically to CXCR4; error bars are standard error of the mean); test substances administered IV except pirfenidone and nintedanib orally

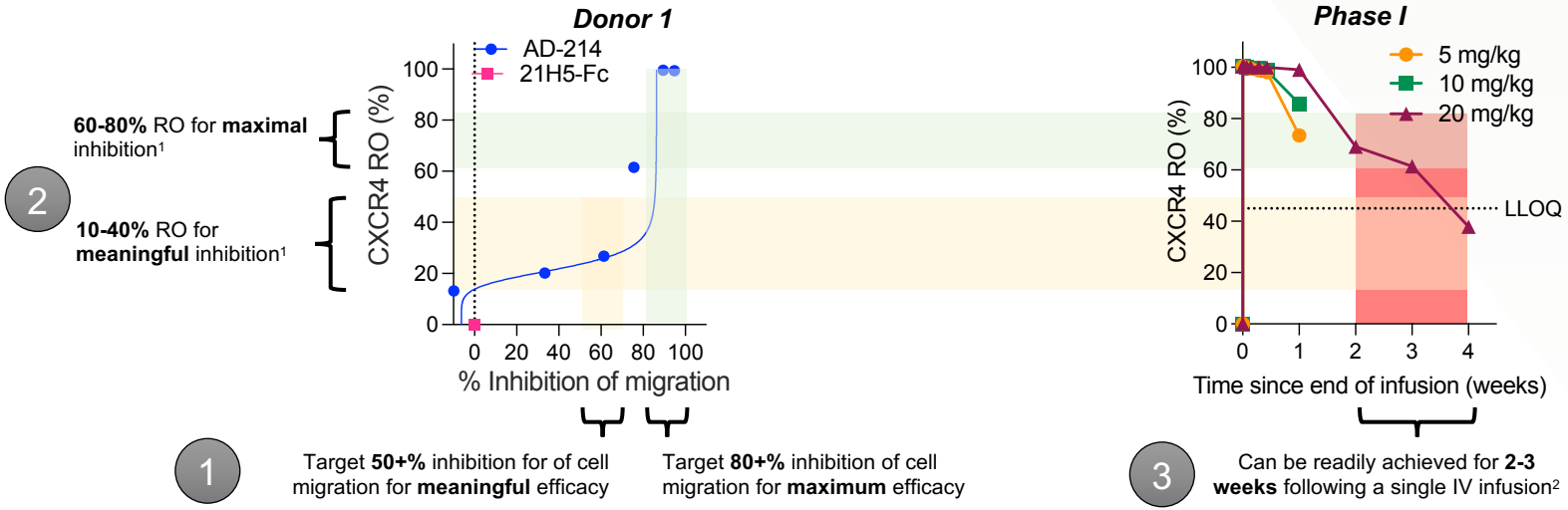
[2] Clinical Study Report: Protocol ID: ADA-AD-214-1A : Version 1 Dated 07 October 2022

Clinically feasible, two weekly IV dosing regimens support sufficient receptor occupancy for to inhibit fibrotic processes

1. ***Ex vivo* cell migration is a model fibrotic process and inhibition of migration is a model of efficacy**
   - Maximum efficacy at >80% inhibition of migration (green). Meaningful efficacy at >50% inhibition (yellow)

2. **Less than full receptor occupancy (CXCR4 RO) is required for efficacy (meaningful inhibition of cell migration)**
   - 60-85% receptor occupancy is sufficient for maximum inhibition of cell migration
   - Meaningful inhibition at receptor occupancy as low as 10-40%

3. **Maintaining efficacious receptor occupancy levels is the objective of dose selection**
   - **Efficacious receptor occupancy can be maintained for at least two weeks after an IV infusion in humans, a clinically viable dosing regimen[2]**



[1] AdAlta studies correlated AD-214 concentration with level of CXCR4 receptor occupancy and level of inhibition of SDF-1α induced migration *ex vivo* on human T cells. Ranges are average of results from three healthy donors, only one donor shown
[2] Clinical Study Report: Protocol ID: ADA-AD-214-1A : Version 1 Dated 07 October 2022

i-body-like sdAb CAR-T therapies are an emerging, validated approach

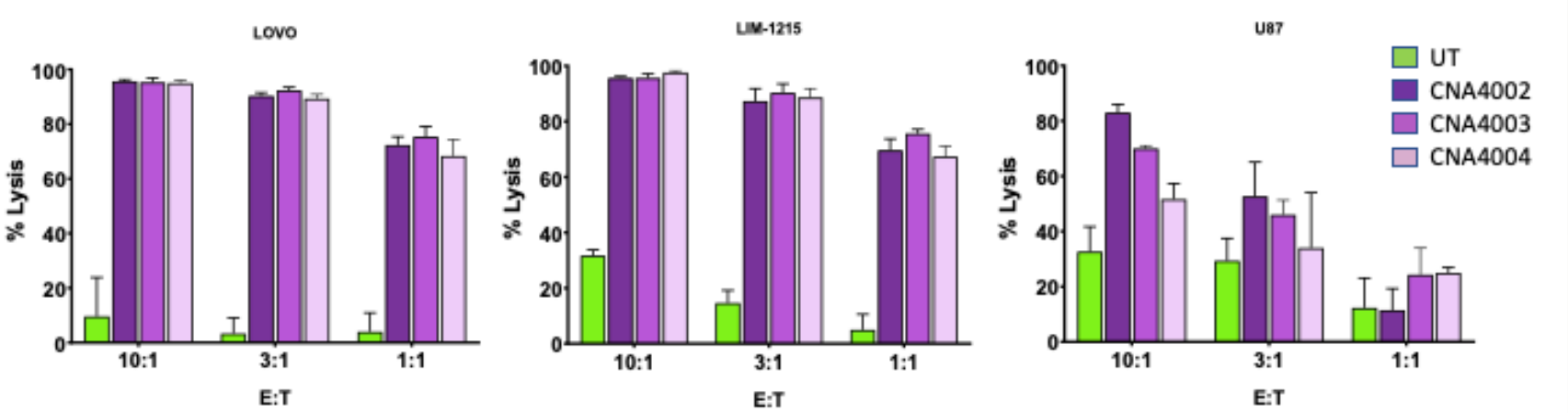
GROUP	YEAR	STAGE	SDAB CAR TARGET	AVAILABLE RESULTS
AdAlta Ltd/Carina Biotech	**2022**	**Proof of principle *(in vitro)***	**Undisclosed**	
Johnson and Johnson[1] Legend Biotech	2022	Market	anti-BCMA CAR-T (biepitopic)	P3 results for n=97 patients ▪ ORR: 97.9%; sCR 78.4% ▪ PFS: 77% (at 12 months) ▪ Overall survival: 89%
Shenzhen Pregene Biopharma[2]	2021	Phase 1 (complete)	anti-BCMA CAR-T	P1 results for n=34 patients: ▪ ORR: 88.2%; sCR/CR: 55.9% ▪ PFS(at 12 months): 53.7%; Median PFS: 12.1 months ▪ Overall survival at 12 months: 78.8%
PersonGen BioTherapeutics[3]	2020	Phase 1 (ongoing)	CD7	P1 results for n=3 patients: ▪ All patients had increased IL-6 ▪ PFS observed in 3/3; remission observed in 2/3 patients
PersonGen BioTherapeutics[4]	2022	Phase 1 (ongoing)	CD19	Not yet available
Legend Biotech[5]	2020	Phase 1 (ongoing)	Claudin 18.2	Not yet available
National Cancer Institute (USA)[6]	2022	Preclinical (mouse)	PD-L1	*In vitro* lysis of breast and liver tumor cells *In vivo* regression of liver tumor cells
Boston Children's Hospital[7]	2019, 2020	Preclinical (mouse)	PD-L1 EIIIB fibronectin	*In vivo* reduction of tumor growth and increased survival Improved activity of CAR-Ts secreting anti-CD47, anti-PD-L1 and anti-CTLA4 nanobodies

[1]https://www.clinicaltrialsarena.com/projects/carvykti-ciltacabtagene-autoleucel/
[2]https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.15_suppl.8025
[3]https://ascopubs.org/doi/10.1200/JCO.2020.38.15_suppl.3026
[4]https://clinicaltrials.gov/ct2/show/NCT04691349?term=car-t+single+domain+antibody&draw=2&rank=1
[5]https://clinicaltrials.gov/ct2/show/NCT04467853
[6]https://www.cell.com/molecular-therapy-family/oncolytics/fulltext/S2372-7705(22)00032-8#secsectitle0020
[7]https://www.pnas.org/doi/10.1073/pnas.1817147116; https://pubmed.ncbi.nlm.nih.gov/32019780/

Building the first iCAR-T cell therapy: proof of principle results

i-body enabled CAR-T (iCAR-T) cells have been successfully generated by Carina and demonstrate *in vitro* cell killing (lysis)[1]

carina biotech AdAlta next generation protein therapeutics



Experimental details

- LOVO and LIM1215 are colorectal cancer cell lines; U87 is a glioblastoma cell line
- 3 different Carina CAR-T constructs incorporating i-body against a single target “X” (CNA4002/CNA4003/CNA4004)
- UT is an unmodified T-cell that does not result in significant killing (lysis) of these cell lines
- i-CAR-T cells manufactured with 97% transduction (i-body CAR insertion) efficiency
- i-CAR-T cells included 60-70% CD4+ (helper) and 20-30% CD8+ (cytotoxic – killer) T cells

1. 210921 Carina iBody Datapack SB (2021) – previously unpublished data